

TRANSMITTAL LETTER TO THE UNITED STATES
DESIGNATED/ELECTED OFFICE (DO/EO/US)
CONCERNING A FILING UNDER 35 U.S.C. 371

20-954

U.S. APPLICATION NO (If known, see 37 CFR 1.5)

09/623181

INTERNATIONAL APPLICATION NO. PCT/GB99/00623	INTERNATIONAL FILING DATE March 2, 1999	PRIORITY DATE CLAIMED March 2, 1998
---	--	--

TITLE OF INVENTION APPARATUS FOR, AND METHOD OF, VARYING THE RATE OF FLOW
OF FLUID ALONG A PATHWAY

APPLICANT(S) FOR DO/EO/US

John Edward Andrew SHAW ✓

Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1. This is a **FIRST** submission of items concerning a filing under 35 U.S.C. 371.
2. This is a **SECOND** or **SUBSEQUENT** submission of items concerning a filing under 35 U.S.C. 371.
3. This express request to begin national examination procedures (35 U.S.C. 371(f)) at any time rather than delay examination until the expiration of the applicable time limit set in 35 U.S.C. 371(b) and PCT Articles 22 and 39(1).
4. A proper Demand for International Preliminary Examination was made by the 19th month from the earliest claimed priority date.
5. A copy of the International Application as filed (35 U.S.C. 371(c)(2))
 - a. is transmitted herewith (required only if not transmitted by the International Bureau).
 - b. has been transmitted by the International Bureau.
 - c. is not required, as the application was filed in the United States Receiving Office (RO/US).
6. A translation of the International Application into English (35 U.S.C. 371(c)(2)).
7. Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3))
 - a. are transmitted herewith (required only if not transmitted by the International Bureau).
 - b. have been transmitted by the International Bureau.
 - c. have not been made; however, the time limit for making such amendments has NOT expired.
 - d. have not been made and will not be made.
8. A translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).
9. An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)).
10. A translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).

Items 11. to 16. below concern document(s) or information included:

11. An Information Disclosure Statement under 37 CFR 1.97 and 1.98.
12. An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.
13. A **FIRST** preliminary amendment.
 - A **SECOND** or **SUBSEQUENT** preliminary amendment.
14. A substitute specification.
15. A change of power of attorney and/or address letter.
16. Other items or information:
 - a. Notification Concerning Submission or Transmittal of Priority Document.
 - b. Notification of Transmittal of the International Preliminary Examination Report.
 - c. International Preliminary Exam Report w/ annexes and amendments.
 - d. Int'l Pub. No. W99/44740.
 - e. International Search Report.
 - f. Notice Informing the Applicant of the Communication of the International Application to the Designated Offices.

17. The following fees are submitted:

BASIC NATIONAL FEE (37 CFR 1.492 (a) (1) - (5)) :

Neither international preliminary examination fee (37 CFR 1.482) nor international search fee (37 CFR 1.445(a)(2)) paid to USPTO and International Search Report not prepared by the EPO or JPO	\$970.00
International preliminary examination fee (37 CFR 1.482) not paid to USPTO but International Search Report prepared by the EPO or JPO	\$840.00
International preliminary examination fee (37 CFR 1.482) not paid to USPTO but international search fee (37 CFR 1.445(a)(2)) paid to USPTO	\$690.00
International preliminary examination fee paid to USPTO (37 CFR 1.482) but all claims did not satisfy provisions of PCT Article 33(1)-(4)	\$670.00
International preliminary examination fee paid to USPTO (37 CFR 1.482) and all claims satisfied provisions of PCT Article 33(1)-(4)	\$96.00

422 Rec'd PCT/PTO 29 AUG 2000

CALCULATIONS PTO USE ONLY

ENTER APPROPRIATE BASIC FEE AMOUNT =

\$ 840

Surcharge of **\$130.00** for furnishing the oath or declaration later than 20 30 months from the earliest claimed priority date (37 CFR 1.492(e)).

\$

CLAIMS	NUMBER FILED	NUMBER EXTRA	RATE	
Total claims	43 - 20 =	23	X \$18.00	\$ 414
Independent claims	13 - 3 =	10	X \$78.00	\$ 780
MULTIPLE DEPENDENT CLAIM(S) (if applicable)			+ \$260.00	\$ 0
TOTAL OF ABOVE CALCULATIONS =				\$ 2034
Reduction of 1/2 for filing by small entity, if applicable. A Small Entity Statement must also be filed (Note 37 CFR 1.9, 1.27, 1.28).				\$
SUBTOTAL =				\$ 2034
Processing fee of \$130.00 for furnishing the English translation later than <input type="checkbox"/> 20 <input type="checkbox"/> 30 months from the earliest claimed priority date (37 CFR 1.492(f)).				\$
TOTAL NATIONAL FEE =				\$ 2034
Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). \$40.00 per property				\$
TOTAL FEES ENCLOSED =				\$ 2034
				Amount to be refunded: \$
				charged: \$

- a. A check in the amount of \$ 2034 to cover the above fees is enclosed.
- b. Please charge my Deposit Account No. _____ in the amount of \$_____ to cover the above fees. A duplicate copy of this sheet is enclosed.
- c. The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 50-0687. A duplicate copy of this sheet is enclosed.
Under Order No. 20-954

NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b)) must be filed and granted to restore the application to pending status.

SEND ALL CORRESPONDENCE TO
 William H. Bollman, Esq.
 Farkas & Manelli, PLLC
 2000 M Street, Suite 700
 Washington, D.C. 20037-3307
 Telephone: 202-261-1020
 Facsimile: 202-887-0336

Date: Aug. 29, 2000

Will H. Boll
 SIGNATURE:
 NAME William H. Bollman
 36,457
 REGISTRATION NUMBER

09/623181
422 Rec'd PCT/PTO 29 AUG 2000
20-954

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

John Andrew Edward SHAW

U.S. Filing Date: **15 August 2000**

U.S. Serial No.: **To be assigned**

International Application No.: **PCT/GB99/00623**

International Filing Date: **2 March 1999**

Title: **APPARATUS FOR, AND METHOD OF, VARYING THE RATE OF FLOW OF FLUID ALONG A PATHWAY**

PRELIMINARY AMENDMENT

Box PCT

Assistant Commissioner for Patents

Washington, D.C. 20231

Sir:

Prior to action in, and calculation of fees for, the above-captioned application, please amend the application as follows:

IN THE CLAIMS:

Please amend the following claims:

Claim 5, line 1, delete "or claim 4".

Claim 6, line 1, change "claims 1 to 5" to --claim1--.

Claim 9, line 1, delete "or 8".

Claim 11, line 1, change "any of claims 7 to 10" to --claim 7--.

Claim 13, line 1, change "any of claims 7 to 12" to --claim 7--.

Claim 14, line 1, change "any of claims 7 to 13" to --claim 7--.

Claim 15, line 1, change "any of claims 7 to 14" to --claim 7--.

Claim 16, line 1, change "any of claims 7 to 15" to --claim 7--.
Claim 17, line 1, change "any of claims 7 to 15" to --claim 7--.
Claim 21, line 1, change "any of claims 18 to 20" to --claim 18--.
Claim 23, line 1, change "any of claims 18 to 22" to --claim 18--.
Claim 24, line 1, change "any of claims 18 to 23" to --claim 18--.
Claim 25, line 1, change "any of claims 18 to 24" to --claim 18--.
Claim 26, line 1, change "any of claims 18 to 24" to --claim 18--.
Claim 27, line 1, change "any of claims 18 to 26" to --claim 18--.
Claim 28, line 1, change "any of claims 18 to 27" to --claim 18--.
Claim 29, line 1, change "any of claims 18 to 28" to --claim 18--.
Claim 30, line 1, change "any of claims 18 to 29" to --claim 18--.
Claim 31, line 1, change "any of claims 18 to 30" to --claim 18--.
Claim 32, line 1, change "any of claims 18 to 31" to --claim 18--.
Claim 33, line 1, change "any of claims 18 to 32" to --claim 18--.
Claim 34, line 1, change "any of claims 18 to 33" to --claim 18--.

REMARKS

By this amendment, the multiple dependencies have been removed from dependent claims 5-6, 9, 11, 13-17, 21, and 23-34 so that each claim depends from a single claim and to avoid the fee charged for such claims as originally presented.

Respectfully submitted,

Aug. 29, 2000


William H. Bollman
Reg. No. 36,457

Farkas & Manelli PLLC
2000 M Street, N.W.
Suite 700
Washington, D.C. 20036-3307
TEL: (202) 261-1020
FAX: (202) 887-0336

09/623181

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

John Edward Andrew SHAW

U.S. Filing Date: **15 August 2000**

U.S. Serial No.: **To be assigned**

International Application No.: **PCT/GB99/00623**

International Filing Date: **2 March 1999**

International Priority Date: **2 March 1998**

Title: **APPARATUS FOR, AND METHOD OF, VARYING THE RATE OF FLOW OF FLUID ALONG A PATHWAY**

December 12, 2000

PRELIMINARY AMENDMENT

Box PCT

Director of US Patent and Trademark Office
Washington, D.C. 20231

Sir:

Prior to action in, and calculation of fees for, the above-captioned application, please amend the application as follows:

IN THE CLAIMS:

Please amend the following claims:

Claim 1, line 1, delete "(10)" and "(14)";

Claim 1, line 2, delete "(14a, 14b)";

Claim 1, line 3, delete "(14)" and "(46)";

Claim 1, line 4, delete "(14b)";

Claim 2, line 1, delete "(10)" and "(14)";

Claim 2, line 2, delete "(14a, 14b)";

Claim 2, line 3, delete "(14)";

Claim 2, line 5, delete "(44)";

Claim 3, line 1, delete "(10)";
Claim 3, line 2, delete "(14b)";
Claim 4, line 1, delete "(10)" and change "any of claims 1 to 3" to – claim 1 –;
Claim 5, line 1, delete "(10)" and "(46)";
Claim 5, line 2, delete "(14b)";
Claim 6, line 1, delete "(10)" and change "any of claims 1 to 5" to – claim 1 –
and delete "(38,40)";
Claim 6, line 3, delete "(48,56)";
Claim 7, line 1, delete "(10)" and change "any of claims 1 to 6" to – claim 1 –;
Claim 8, line 1, delete "(10)" and change "any of claims 1 to 7" to – claim 1 –;
Claim 9, line 1, delete "(10)" and change "any of claims 1 to 7" to – claim 1 –;
Claim 10, line 1, delete "(10)" and change "any of claims 1 to 9" to – claim 1 –;
Claim 10, line 2, delete "(80)";
Claim 11, line 1, delete "(10)" and change "any of claims 1 to 10" to – claim 1 –;
Claim 12, line 1, delete "(10)" and change "any of claims 1 to 11" to – claim 1 –;
Claim 13, line 1, delete "(10)" and change "any of claims 1 to 12" to – claim 1 –;
Claim 14, line 1, delete "(10)" and change "any of claims 1 to 13" to – claim 1 –;
Claim 14, line 2, delete "(12)", "(14)" and "(16)";
Claim 14, line 3, delete "(18)" and "(20)";
Claim 14, line 4-5, delete "(22)", "(26,28,30,32)" and "(11,13)";
Claim 15, line 1, delete "(10)" and change "any of claims 1 to 14" to – claim 1 –;
Claim 16, line 1, delete "(10)" and change "any of claims 1 to 15" to – claim 1 –;
Claim 17, line 1, delete "(10)" and change "any of claims 1 to 16" to – claim 1 c
Claim 18, line 1, delete "(10)" and "(14)";
Claim 18, line 2, delete "(14a, 14b)";
Claim 18, line 3, delete "(14)" and "(46)";
Claim 18, line 4, delete "(14b)";
Claim 19, line 1, delete "(10)" and "(14)";
Claim 19, line 2, delete "(14a, 14b)";
Claim 19, line 3, delete "(14)";

Claim 19, line 4, delete "(44)";
Claim 20, line 1, delete "(10)" and change "any of claims 1 to 19" to – claim 1 –;
Claim 20, line 2, delete "(14a)";
Claim 20, line 3, delete "(14)";
Claim 20, line 4, delete "(44)";
Claim 20, line 5, delete "(10)";
Claim 21, line 1, delete "(10)";
Claim 21, line 2, delete "(14a)";
Claim 22, line 1, delete "(10)";
Claim 22, line 2, delete "(14)";
Claim 23, line 1, delete "(10)";
Claim 23, line 2, delete "(44)";
Claim 24, line 1, delete "(10)";
Claim 25, line 1, delete "(75)";
Claim 25, line 2, delete "(75)" and "(78)";
Claim 26, line 1, delete "(75)";
Claim 26, line 2, delete "(75)" and "(78)";
Claim 27, line 1, delete "or 26";
Claim 29, line 1, change "any of claims 25 to 28" to – claim 25 – and delete
"(72)";
Claim 29, line 2, delete "(75)";
Claim 30, line 1, delete "(72)" and "(74)";
Claim 31, line 1, change "any of claims 25 to 30" to – claim 25 –;
Claim 31, line 2, delete "(76)";
Claim 32, line 1, change "any of claims 25 to 31" to – claim 25 –;
Claim 33, line 1, change "any of claims 25 to 32" to – claim 25 –;
Claim 34, line 1, change "any of claims 25 to 33" to – claim 25 – and delete
"(78)";
Claim 35, line 1, change "any of claims 25 to 33" to – claim 25 – and delete
"(78)";

Claim 36, line 1, change "any of claims 25 to 30" to – claim 25 –;

Claim 36, line 2, delete "(76)";

Claim 37, line 1, delete "(75)";

Claim 37, line 2, delete "(75)" and "(78)";

Claim 37, line 4, delete "(76)";

Claim 38, line 1, delete "(75)";

Claim 38, line 2, delete "(75)" and "(78)";

Claim 38, line 4, delete "(76)";

Claim 39, line 1, delete "(75)";

Claim 39, line 2, delete "(72)" and "(75)";

Claim 39, line 3, delete "(78)";

Claim 40, line 2, delete "(72)" and "(75)";

Claim 40, line 3, delete "(78)";

Claim 41, line 1, delete "(75)";

Claim 41, line 2, delete "(75)" and "(78)";

Claim 41, line 3, delete "(75)";

Claim 41, line 4, delete "(78)";

Claim 42, line 1, delete "(75)";

Claim 42, line 2, delete "(75)" and "(78)";

Claim 42, line 4, delete "(78)";

Claim 43, line 1, delete "or claim 42";

Claim 44, line 1, change "claims 39 to 42" to – claim 39 – and delete "(78)";

Claim 45, line 1, delete "(75)";

Claim 45, line 2, delete "(72)" and "(75)";

Claim 45, line 3, delete "(78)";

Claim 46, line 2, delete "(72)" and "(75)";

Claim 46, line 3, delete "(78)";

Claim 47, line 1, delete "(75)";

Claim 47, line 2, delete "(75)" and "(78)";

Claim 47, line 3, delete "(75)";

Claim 47, line 4, delete "(78)";
Claim 48, line 1, delete "(75)";
Claim 48, line 2, delete "(75)" and "(78)";
Claim 48, line 4, delete "(78)";
Delete claim 49;
Delete claim 50;
Delete claim 51;
Delete claim 52.

REMARKS

By this amendment, the multiple dependencies have been removed from dependent claims 3-17, 20-24, 27-36, 43 and 44 so that each claim depends from a single claim and to avoid the fee charged for such claims as originally presented.

Respectfully submitted,



William H. Bollman
Reg. No. 36,457

Farkas & Manelli PLLC
2000 M Street, N.W.
Suite 700
Washington, D.C. 20036-3307
TEL: (202) 261-1020
FAX: (202) 887-0336

ART 34 AMDT

422 Rec'd PCT/PTO 29 AUG 2000

1

APPARATUS FOR, AND METHOD OF, VARYING THE RATE OF FLOW OF FLUID ALONG A PATHWAY

5 Technical Field

This invention relates to an apparatus for and method of varying the rate of flow of a fluid along a pathway. More particularly, but not exclusively, the invention varies the rate of flow of fluid along a pathway in a wet chemistry analysis system.

10 Background Art

A common feature of all "wet chemistry" analysis or assay systems is that analyte, together with one or more reagents, usually passes through a series of processes or procedures. These include: mixing, reacting, incubating, filtering, decanting, metering and dividing. In short, some form of fluid handling is a common and important feature of most assay systems.

International Patent Application WO-A1-9419484 (Biocircuits Corporation) describes a disposable device for use in diagnostic assays and comprises a number of chambers and interconnecting pathways. Capillary valves are used to enhance control over fluid flow in the device. One type of capillary valve comprises a fluid flow capillary channel and a control capillary channel which intersect each other at right angles. The intersection disrupts fluid flow in the flow capillary channel when the control capillary is empty, but does not impede flow through the flow capillary channel when it is full. Thus, fluid flow through the device can be controlled by either filling or emptying the control capillary with liquid.

A similar disposable device is described in International Patent Application WO-A1-9727324 (David Sarnoff Research Center). This device uses valves and pumps for controlling the flow of fluid. The valves used may be of the plunger type such that the valve has a piston and plunger rod. The diameter of the plunger rods is typically of the order of 60 μm and the piston diameter is typically of the order of 200 μm .

In US Patent No. 5,267,585 (BOC Health Care), a flow control valve is disclosed. A deformable elastomeric element is positioned at least partially within the flow path of a

AMENDED SHEET

ART 34 AMDT

1a

fluid passing between an inlet and an outlet. By deforming the elastomeric element, the cross-section of the flow path of the fluid is changed, thereby controlling the flow of fluid through the flow control valve.

- 5 A temperature operated gas valve is described in US Patent No. 4,949,742 (Spectra-
Physics). The valve includes a conduit positioned between high and low pressure gas
regions. Within the conduit is a restriction, and this restriction is closed by a meltable solid
material. When the valve is to be opened, heat is applied to the meltable solid material,
causing some of the material to flow and allow the passage of gas from the higher pressure
10 region to the lower pressure region. When the pressure between the two regions has
substantially equalized, surface tension associated with the restriction in the conduit pulls
the liquified material back into place to close and reseal the valve.

- 15 A capillary transport device having an internal capillary transport passage is disclosed in
US Patent No. 4,549,952 (Eastman Kodak). To control the liquid flow rate in the passage,
a water-swellable composition (such as gelatin or starch) is used.

- International Patent Application WO-A1-9822625 (University of Michigan/Becton
Dickinson) discloses methods and compositions for isothermal amplification of nucleic
20 acids in a micro-fabricated device. The device includes fluid channels connected to an
isothermally regulated reaction chamber. Fluid flow in the channels may be regulated by
the use of meltable materials placed in or alongside the channels.

- 25 In US Patent No. 5,278,079 (Enzymatics Inc.) a diagnostic device having capillary tubes is
described. The capillary tubes contain a volume of water-expandable polymer which forms

a seal in the tubes when it is in contact with an aqueous medium. However, once sealed, the capillary tubes cannot be easily reopened.

In conventional analysis techniques, fluid handling relies on precisely engineered fluid controllers such as valves, taps and fluid delivery systems. These fluid controllers are expensive and difficult to manufacture. They are therefore not appropriate for inclusion in disposable units due to their number and cost.

An aim of the present invention is to overcome the aforementioned problems by providing
10 a means for varying the flow of fluid along a pathway.

Disclosure of Invention

According to a first embodiment of the invention there is provided a method of varying the rate of fluid flow along a pathway comprising the steps of: providing at least one recess located substantially adjacent the pathway; locating a plug of deformable material in the pathway so that the material substantially restricts the flow of fluid in the pathway; and changing the state of the deformable material so that at least a portion of the material passes into the at least one recess thereby permitting flow of the fluid along the pathway.

20 According to a second embodiment of the invention there is provided method of varying the rate of fluid flow along a pathway comprising the steps of: providing at least one recess located substantially adjacent the pathway; locating a volume of deformable material in the at least one recess; and changing the state of the deformable material so that at least a portion of the material passes into the pathway thereby substantially restricting flow of the
25 fluid along the pathway.

According to a third embodiment of the invention there is provided a method of varying the rate of fluid flow along a pathway comprising the steps of: providing a pathway; locating a volume of deformable material in the pathway so that it substantially restricts the flow of fluid along the pathway; and changing the state of the deformable material so that at least a portion of the material passes along a predetermined path thereby permitting flow of the fluid along the pathway.

According to a fourth embodiment of the invention there is provided a method of varying the rate of fluid flow along a pathway comprising the steps of: providing a pathway; locating a volume of deformable material in the pathway so that it substantially permits the flow of fluid along the pathway; and changing the state of the deformable material so that at least a portion of the material passes along a predetermined path thereby substantially restricting flow of the fluid along the pathway.

Preferably the predetermined path is defined by one or more regions that repels or attracts the deformable material. A region having such a property is hereinafter referred to as being hydrophobic.

The state of the deformable material may be changed by applying to the deformable material (i) heat, (ii) pressure, (iii) uv radiation, (iv) light, (v) ultrasonic energy or a combination of any of (i) to (v).

According to a further embodiment of the invention there is provided an apparatus for varying the rate of fluid flow along a pathway, the apparatus including at least one pathway and a volume of deformable material disposed within the pathway whereby, in use, a change of state of the deformable material causes a change of the rate of fluid flow along the pathway.

According to another embodiment of the invention there is provided an apparatus for varying the rate of fluid flow along a pathway, the apparatus including at least one pathway and a volume of deformable material disposed adjacent the pathway whereby, in use, a change of state of the deformable material causes a change of the rate of fluid flow along the pathway.

The apparatus may also include at least one chamber in fluid connection with one or more pathways. A volume of deformable material may be disposed within the at least one chamber.

4

At least one recess capable of receiving deformable material is preferably located substantially adjacent the at least one pathway. The at least one recess may have an opening which acts as a vent in order to permit the flow of gas therethrough.

- 5 The apparatus may also include at least one hydrophobic region. Thus the flow of material is guided along a predetermined path and discouraged from contacting other regions of the pathway, chamber, or device.

The apparatus may include means for the supply and/or removal of heat from the apparatus
10 in order to increase or decrease the rate of change of state of the deformable material. When heat (or other form of energy) is applied to a region of the apparatus containing the deformable material, the material may change its position, size, state or function. This causes a rate of change in the fluid flow in the pathway. Thus a pathway which is initially obstructed becomes unobstructed, and vice versa.

15 Heater elements may be printed onto the apparatus or a heating tool may be used to apply heat to local areas of the apparatus. Alternatively, heat may be applied to or removed from larger regions of the apparatus, or to a device which includes the apparatus. For example, by dipping into a water bath, heating with an external heater, or by a Peltier.

20 The apparatus may also include means for the supply of pressure, uv radiation, light, ultrasonic energy, or other suitable means for changing the state of the deformable material.

25 The deformable material may be a thermally activated material. Preferably the thermally activated material is wax, contains or is a polymer such as polypropylene polystyrene, a wax/polymer mix, a metal such as Indium, or any other suitable low melting point material that changes its state on application of heat, and on cooling. The terms thermally activated material and wax are hereinafter used interchangeably.

30

In summary, fluid flow along a pathway of the apparatus is varied by way of valves, or clamps, which are preferably formed from a deformable material. The valves and clamps

may be opened and/or closed upon the application of heat, pressure, or other suitable means. The valves and clamps may also be known as gates. Hereinafter, a gate that opens a pathway to the flow of fluid on application of heat is known as a heat openable gate. A gate that closes a pathway to the flow of fluid on application of heat is known as a heat closable gate.

One example of a heat openable gate has thermally activated material situated in the pathway so as to enable the material in its melted state to flow into at least one recess substantially adjacent the pathway. Air (or other gas) is displaced from the recess by the material and exits through a vent. A type of heat closable gate has thermally activated material situated in at least one recess substantially adjacent the pathway. As the material in its melted state flows from the recess into the pathway, it is replaced by air (or other gas) via the vent.

15 Alternatively, (or in addition to the material being situated in at least one recess), the material may be situated in the fluid pathway such that the pathway is either substantially or partially obstructed. If the thermally activated material is substantially obstructing the pathway, then the pathway may be opened to the flow of fluid by applying heat to the material. This is a form of heat openable gate. However, if the material is situated so as not to, or only partially, obstruct the flow of fluid, on application of heat the material melts 20 and flows so as substantially obstruct the pathway. This is a form of heat closable gate.

In a further alternative embodiment, thermally activated material may be arranged to contact at least two points on inner surfaces of the apparatus, forming a clamp. Clamps 25 may be situated in chambers. Upon application of heat to a clamp, the clamp melts, and surfaces of the chambers are separated. Thus a pressure differential is provided to drive fluid along pathways and into, or from, chambers.

30 Preferably at least one surface contained within the apparatus is resiliently deformable. This is advantageous because it means that if the surfaces are constructed from sufficiently pliable materials, pressure may be applied to a surface, and the surfaces will return to their original state.

may be opened and/or closed upon the application of heat, pressure, or other suitable means. The valves and clamps may also be known as gates. Hereinafter, a gate that opens a pathway to the flow of fluid on application of heat is known as a heat openable gate. A gate that closes a pathway to the flow of fluid on application of heat is known as a heat closable gate.

One example of a heat openable gate has thermally activated material situated in the pathway so as to enable the material in its melted state to flow into at least one recess substantially adjacent the pathway. Air (or other gas) is displaced from the recess by the material and exits through a vent. A type of heat closable gate has thermally activated material situated in at least one recess substantially adjacent the pathway. As the material in its melted state flows from the recess into the pathway, it is replaced by air (or other gas) via the vent.

15 Alternatively, (or in addition to the material being situated in at least one recess), the material may be situated in the fluid pathway such that the pathway is either substantially or partially obstructed. If the thermally activated material is substantially obstructing the pathway, then the pathway may be opened to the flow of fluid by applying heat to the material. This is a form of heat openable gate. However, if the material is situated so as not to, or only partially, obstruct the flow of fluid, on application of heat the material melts 20 and flows so as substantially obstruct the pathway. This is a form of heat closable gate.

In a further alternative embodiment, thermally activated material may be arranged to contact at least two points on inner surfaces of the apparatus, forming a clamp. Clamps 25 may be situated in chambers. Upon application of heat to a clamp, the clamp melts, and surfaces of the chambers are separated. Thus a pressure differential is provided to drive fluid along pathways and into, or from, chambers.

Preferably at least one surface contained within the apparatus is resiliently deformable. 30 This is advantageous because it means that if the surfaces are constructed from sufficiently pliable materials, pressure may be applied to a surface, and the surfaces will return to their original state.

Pathways may contain a volume of material so that upon application of pressure, a rate of change of fluid flow in the pathway occurs. The material may be thermally activated. Thus for a heat closable pathway, a tool may be used to seal the pathway by connecting the upper and lower surfaces with the thermally activated material. Thermally activated material may not be required if the upper and lower surfaces of the pathway may be directly connected to one another. For a heat openable pathway, a tool may make a channel in the wax contained in the pathway. When this occurs the resiliently deformable material of the pathway returns to a previous state. Pathways opened in this way may be resealed by heating and subsequent cooling of the wax.

10

Preferably the volumes of deformable material may be accessed independently and sequentially to precisely control the path of fluid flow in the apparatus.

Valves and clamps may be single use structures, or may be reusable.

15

The invention may be incorporated into a chemical assay device. The assay device preferably has at least one chamber in fluid connection with at least one pathway, the pathway being adapted to allow fluid to flow to or from said chamber, characterised in that there is provided a volume of deformable material in the pathway whereby, in use, a change of state of the deformable material causes a change of the rate of fluid flow along the pathway.

20
25 The deformable material may be situated in the pathway such that the pathway is substantially obstructed or, alternatively, the material may be situated in the pathway such that the pathway is only partially obstructed.

At least one recess may be located substantially adjacent the pathway, the recess being capable of receiving the deformable material.

30 According to another embodiment of the invention, the assay device preferably has at least one chamber in fluid connection with at least one pathway, the pathway being adapted to allow fluid to flow to or from said chamber, characterised in that there is provided a volume of deformable material situated in a recess, the recess being located substantially

adjacent the pathway whereby, in use, a change of the deformable material causes a change of the rate of fluid flow along the pathway.

An opening may be provided in the recess which acts as a vent.

5

The chamber may comprise a deformable envelope and at least two points on the envelope may be connected by way of a volume of deformable material.

A region of the device may have at least one hydrophobic portion so that the flow of the
10 deformable material is guided along a predetermined path.

Preferably the deformable material is thermally deformable. The material may, however,
be mechanically deformable.

15 The device may include heating means for melting the thermally deformable material. The device may also include means for removing heat such as, for example, a heat sink. Heat may selectively be applied and/or removed from individual wax gates and/or clamps.

20 Preferably at least one surface defined by or in the device is resiliently deformable so that the wax gates and/or clamps may be mechanically deformed.

The device may have at least one component from the set of: an inlet port, a reaction chamber, a waste depot, a filter chamber, an infinity capture and processing chamber, a wash solution/reagent reservoir, an array of metered readout cells, and a breather tube.

25

The assay device is usually rectangular, but other shapes are equally viable, such as discs or hexagons. Depths of fluid pathways and chambers may be sufficiently narrow to allow filling by capillary action (say 0.02 to 0.2 mm). Pathways may be wider (of the order of a millimeter) where the fluid flow is to be propelled by gravity, a pressure impulse,
30 centrifugal force, or an inertial force. The aforementioned dimensions are consistent with processing fluid samples in the range of approximately 30 to 50 microlitres, and are given by way of example only.

According to a further embodiment of the invention there is provided a method of manufacturing an assay device, the method including the steps of: a) defining at least one fluid pathway on a substrate; b) defining at least one reaction chamber on a substrate; c) forming at least one component composed of a deformable material in the device; and d) bonding together at least two substrates to form the device.

The body of the assay device is preferably formed from a polymer or from a combination of materials including glass, ceramics, or metal. Construction may involve injection moulded components, and/or the joining together of a number of laminae. Pathways and chambers in the assay device may be formed in a plane defined between upper and lower planar sheets. Pathways and chambers may be formed by printing, etching, ablation, cutting of the substrate, moulding of a substrate, or a combination of these. More complex structures may be realised by building up laminae and providing vias for the flow of fluids between adjacent levels.

Bonding of upper and lower portions of the device is critical for its operation. Bonding can be achieved by means of screen printed adhesives containing for example spacer balls, by cut adhesive gasket materials, by heating sealing, by uv curing, by mechanical fixing, by ultrasonic bonding, or by using a porous-gasket technique, for example as described in US-A-4,865,716.

The assay device may include one or more of the aforementioned gates, valves or clamps. Preferably each individual gate, valve and/or clamp may be accessed independently one from another.

Wax gates and clamps may also be printed using molten wax or wax dissolved in a solvent, by injection of molten wax into the device using feeder tubes, by etching of the device, or by placing individual wax elements within the apparatus using pick and place equipment.

Provision may be made for fluid overflow lines, for collection of waste, and for opening and sealing of the device at stages from start of use until disposal.

Brief Description of Figures

Embodiments of the invention will now be described by way of examples, and with reference to the accompanying Figures in which:-

- 5 Figure 1 is a schematic plan view of a chemical assay device incorporating the invention;

Figure 2a is a plan view of a pathway having an initially open wax gate, where wax is situated in recesses adjacent the pathway;

- 10 Figure 2b shows a plan view of the pathway of Figure 2a, where the wax gate has been closed upon the application of heat to the gate;

Figure 3a shows a plan view of a pathway having an initially open wax gate, where a volume of wax is situated in the pathway;

- 15 Figure 3b shows a plan view of the pathway of Figure 3a, where the wax gate has been closed upon the application of heat to the gate;

Figure 4a shows a plan view a pathway having an initially open wax gate, where a volume of wax is situated in the pathway;

- 20 Figure 4b shows a cross-section of the pathway of Figure 4a;
Figure 4c shows a cross-section of the pathway of Figure 4a, the pathway having been closed on application of heat and pressure;

Figure 5a shows a plan view of a pathway having an initially closed wax gate, where wax is situated in the pathway, and recesses adjacent the pathway;

- 25 Figure 5b shows a plan view of the pathway of Figure 5a, where the wax gate has been opened upon the application of heat to the gate, wax having flowed into the recesses adjacent the pathway;

- 30 Figure 6a shows a plan view of a pathway having an initially closed wax gate, where a volume of wax is situated in the pathway;

Figure 6b shows a plan view of the pathway of Figure 6a, where the wax gate has been opened upon the application of heat to the gate;

10

Figure 7a shows a cross-section of a pathway having a wax gate which has been closed, and a heating tool;

Figure 7b shows a cross-section of the pathway of Figure 7a, where the pathway has been reopened to the flow of fluid upon application of heat and pressure;

5 Figure 7c shows a plan view of Figure 7b;

Figure 8a shows a plan view of a wax clamp used in a chamber, in which the clamp may be initially closed or open;

Figure 8b shows a cross-section of an deflated chamber having a wax clamp;

Figure 8c shows a cross-section of an inflated chamber having a wax clamp;

Figure 9a shows a plan view of a chamber containing a gas generating mixture in fluid connection with a pathway having an initially closed wax gate;

Figure 9b shows a plan view of the chamber of Figure 9a having an opened wax gate where fluid has flowed into the chamber (under capillary action or external pressure), and is in contact with the gas producing material contained within the chamber;

Figure 9c shows a plan view of the chamber of Figure 9a where fluid has been driven out of the chamber by a gas; and

Figure 9d shows a cross-section of the chamber and connecting pathway of Figure 9a.

20

Detailed Description of Preferred Embodiments

The embodiments of the invention shown in Figures 2 to 9 may be incorporated into the chemical assay device of Figure 1, or they may be included in other types of assay (or other) devices.

25

Referring to Figure 1, there is shown a chemical assay device 10 for analysis of blood, or other biological fluid. End products of a reaction or assay may be detected using optical methods. For example, a colour change may be detected by a photo-diode, or a fibre-optic system, or visually. The device has an area typically about 50 cm^2 and is 3 to 10 millimetres thick. The device 10 may be significantly larger or smaller depending on the complexity of the processes to be carried out and the volumes of fluids to be processed. In this particular embodiment, the assay device 10 is configured to carry out an

immunological assay and this will be described so as to illustrate a method of operation of the invention.

Assay device 10 comprises a generally square, substantially planar substrate in which a number of chambers are interconnected by pathways. Fluid control in the device 10 is by way of wax gates and clamps, which are shown in Figure 1 in their initial (open or closed) states.

The device 10 includes an inlet port 12 in fluid connection with a reaction (e.g., lysing) chamber 14 via a pathway 12a. Chamber 14 leads to waste depot 16 and filter chamber 18 via separate fluid channels 14a and 14b respectively. Filter chamber 18 is in fluid connection with chambers 22 and 24 via respective fluid channels 18a and 18b, and with processing chamber 20. Chamber 22 is initially filled with a wash solution, and chamber 24 is filled with an eluent which is used to displace material from processing chamber 20.

15

Processing chamber 20 is connected to waste depot 16 via a channel 20a. Channel 20a leads to an array of metered read-out cells 26, 28, 30 and 32. Air from read-out cells 26 to 32 exits into channel 16a. A channel 16b is provided and links channels 20a and 16a. The operation of one of the metered readout cells will now be explained with reference to readout cell 26 of Figure 1.

A region of the analysis area of device 10 comprises a large-bore inlet port 26a leading to a fixed-volume cell 26, which in turn is connected to a narrow-bore outlet tube 26b. Tube 26b leads to pathway 16a, and ultimately to waste depot 16. The structure comprising parts 26a, 26 and 26b has a fluid impedance which is dependent on the amount of fluid therein. Fluid can flow freely into the cell until the narrow-bore section is reached, at which stage the force needed to continue driving the fluid into the cell is greatly increased. At this point the fluid, which flows most readily along the path of least resistance, diverts to the conduit leading to the next cell (28 in this case), and so on. Thus each of the cells 26, 28, 30, 32 is filled in turn, and the volume of fluid entering each cell can be controlled.

12

Chamber 20 is also connected to chamber 38 via a fluid pathway 20b, and chamber 38 leads to chamber 40. Chambers 38 and 40 both contain wax clamps. Both chambers 38 and 40 are initially deflated.

5 Waste depot 16 connects to breather tube 13 via pathway 16c, and reservoir 22 leads to breather tube 11 via pathway 22a. Breather tubes 11 and 13 ensure that fluid moves freely within the device. Also tubes 11 and 13, when connected to non-critical regions, ensure that any excess fluid does not interfere with any on-going analysis.

10 Reservoir 24 is connected to chamber 42 via pathway 24a. Chamber 42 is pre-filled with a dry mixture which, when in contact with a liquid, produces a gas. This is shown diagrammatically in Figure 9.

15 Wax gates are situated in fluid pathways in order to control flow of fluid between the chambers. In Figure 1, gates are shown in their initial states. For example, fluid flow is initially obstructed at gate 34, whereas initially fluid is allowed to flow freely through gate 36.

20 Referring again to Figure 1, a typical sequence of events for an immunological assay is now described. A blood sample (not shown) is injected into the assay device via inlet port 12. Blood fills reaction chamber 14 by capillary action and/or hydrostatic pressure, and excess blood enters the waste depot 16 via pathway 14a. The blood remains in chamber 14 for as long as is required for cell lysing to occur with a reagent. The reagent is introduced into this chamber in a predetermined dose during the manufacture of the device. Heat is 25 then applied to gates 44, 46 and clamp 48 in order to close gate 44, open gate 46, and release clamp 48 thereby actuating partial vacuum chamber 38.

The lysed blood is then urged through filter chamber 18 by way of a partial vacuum, and serum fills processing chamber 20. An antigen in the blood serum then bonds to an antibody which has been tagged onto, for example, glass or ceramic beads (not shown). 30 The beads are pre-dosed and introduced in chamber 20 at the manufacturing stage.

13

The serum is then washed from the glass beads in chamber 20 by activating heaters at gates 50, 52 and 54, and clamp 56. A partial vacuum in chamber 40 draws wash fluid from chamber 22 through chamber 20 leaving the antigen bound to the particles in chamber 20. Waste wash solution and serum enter chambers 38 and 40.

5

The next step is elution. Activating heaters placed at gates 57, 58, 60, 36, 34 and 62 allow the fluid in the reagent reservoir 24 to wet a gas producing powder. Fluid is then driven by the gas through chamber 20 towards analysis cells 26, 28, 30 and 32. As eluent from reservoir 24 passes through chamber 20, antigen is released from the beads and carried in the eluent to the analysis cells. These cells contain reagents such as enzyme systems which react with the antigen, causing either a colour change in the solution, or a change in fluorescence. Any recognised method of optical analysis can then be used for detection and measurement of end products of the reactions. Once cells 26, 28, 30 and 32 are filled, resistance to fluid flow increases in the narrow exit channels 26b, 28b, 30b, and 32b.

10 Excess fluid is then expelled to waste depot 16 through channel 16b.

15

Finally, activating heaters at gates 66, 68 and 70 seal the fluids within the device for hygienic disposal.

20 Further embodiments of the invention are described now with reference to Figures 2 to 9 inclusive.

Figure 2 shows a plan view of a section of a pathway having a wax gate 73 that closes the pathway to the flow of fluid on application of heat. A volume of wax is contained in recess 72. Pathway 75 has a region of hydrophobicity 76 in order to guide the flow of wax. Upon application of heat to gate 73, the wax melts and flows (guided by the hydrophobic region) into the fluid pathway to obstruct the flow of fluid therein. Air enters through inlet 74 and replaces the wax in recess 72. Thus air prevents flowback of the molten wax. As the wax cools, fluid flow along the pathway becomes obstructed.

30

In Figure 3 a plan view of a section of pathway having a wax gate 77 is shown. Gate 77 closes pathway 75 to the flow of fluid on application of heat to the gate. A volume of wax 78 is situated in the path of the fluid, only partially obstructing the fluid flow. Upon

14

application of heat to the gate, the wax melts and flows to block the pathway guided by the area of hydrophobicity 76. As the wax cools fluid flow along the pathway becomes obstructed.

- 5 Figure 4 shows another form of heat closable pathway. A volume of wax 78 is situated in pathway 75, only partially obstructing the flow of fluid. In order to block the channel, a moveable heat sealing tool 80 is used to apply both pressure and heat, completely sealing the channel. This form of gate requires that at least one sheet forming the pathway is formed from deformable material. If the deformable material can be directly sealed to the 10 second sheet (by heat, pressure or otherwise), then wax is not required.

Figures 5, 6 and 7 all represent forms of heat openable pathways, that is, wax gates that are initially closed to fluid flow in the pathway.

- 15 Figure 5 shows a plan view of a section of a pathway 75 having a gate 79 that opens the pathway to the flow of fluid on application of heat to the gate. A volume of wax is situated in the pathway between two recesses 72. The recess has a region of hydrophobicity 76 in order to guide the flow of wax. Upon application of heat to the gate, the wax melts and flows into the recess. Air exhausts via inlet 74 and is replaced by the wax in the recess, preventing flowback of the molten wax. As the wax cools the fluid pathway opens.
20

Referring to Figure 6, there is shown a plan view of a section of pathway 75 having another form of wax gate 81. The gate opens the pathway to the flow of fluid on application of heat to the gate. A volume of wax 78 is situated in the path of the fluid preventing fluid flow. Upon application of heat to this wax gate, the wax melts and flows in the pathway guided by the area of hydrophobicity 76. As the wax cools, the fluid pathway permits fluid to flow along the pathway.
25

- Figure 7 shows another heat openable gate situated in pathway 75. A volume of wax 78 is situated in the pathway, obstructing the flow of fluid. In order to open the pathway to allow the flow of fluid, a moveable heat sealing tool 80 is used to apply both pressure and heat to the pathway. The shape of this heat sealable tool allows the wax to be deformed, forming a channel in the wax. This type of gate requires that at least one sheet forming the pathway is
30

deformable and resilient, so that the sheet may return to its original state and leave the pathway open.

In addition to the aforementioned wax valves, components to actuate fluid flow may be required. Capillary action may be used to provide some fluid movement, and this can be extended by opening further fillable or absorbent areas or by opening valves of the types previously described. However, greater flexibility is achieved by employing structures capable of generating pressure differentials, and these are shown in Figures 8 and 9.

- 10 Figure 8 shows a chamber 38 containing a wax clamp 78. Changing the shape and volume of chamber 38 provides a pressure differential to drive (or suck) fluid in the connected pathways and chambers. Two sheets of synthetic plastics material 37a and 37b are fixed together using a volume of wax 78 in order to produce a deflated chamber 38. Upon application of heat, wax clamp 78 melts. This allows the surfaces of chamber 38 to separate thereby inflating the chamber. This results in a pressure change and fluid is sucked through interconnecting pathways. Chamber 38 may be returned to its deflated state by the application of an external pressure (shown in the direction of arrow A) and by heating the wax. As the wax cools, the deformable surfaces are fixed together.
- 15
- 20 Figure 9 shows a further means of generating pressure in order to drive the flow of fluid. Figure 9 shows a chamber 88 connected to a pathway having a closed wax gate 86. The chamber contains a dry gas generating mixture 82, for example sodium bicarbonate with tartaric acid. On applying heat to the wax gate 86, the wax flows to unblock the pathway 85. A solution 84 flows into the chamber 88, wetting the gas generating mixture and causing the generation of a gas. The gas increases the pressure inside the chamber, ejecting the liquid that has flowed into the chamber and propelling it along one or more interconnecting pathways. In addition to the gas generating mixture, an inert absorbent material may be included in the chamber, or the chamber may be filled with capillary matting which acts as a wick.
- 25
- 30 The invention has been described by way of a number of embodiments, and it will be appreciated that variation may be made to these embodiments without departing from the scope of the invention.

ART 34 AMDT 09 / 623181

16

422 Rec'd PCT/PTO 29 AUG 2000

Claims

1. An assay device (10) having at least one chamber (14) in fluid connection with at least one pathway (14a, 14b), the pathway being adapted to allow fluid to flow to/from said chamber (14), characterised in that there is provided a volume of deformable material (46) in the pathway (14b), which, in use, changes its state so as to cause a change of the rate of fluid flow along the pathway.
2. An assay device (10) having at least one chamber (14) in fluid connection with at least one pathway (14a, 14b) the pathway being adapted to allow fluid to flow to/from said chamber (14), characterised in that there is at least one recess located substantially adjacent the pathway and, situated in the recess, there is provided a volume of deformable material (44) which, in use, changes its state so as to cause a change of the rate of fluid flow along the pathway.
3. An assay device (10) according to claim 1 wherein there is at least one recess located substantially adjacent the pathway (14b).
4. An assay device (10) according to any of claims 1 to 3 wherein an opening is provided, the opening acting as a vent to or from the recess.
5. An assay device (10) according to claim 1 wherein the deformable material (46) is situated in the pathway (14b) such that the pathway is partially obstructed.
6. An assay device (10) according to any of claims 1 to 5 wherein the chamber (38,40) comprises a deformable envelope and at least two points of the envelope are connected by way of a volume of deformable material (48,56).
7. An assay device (10) according to any of claims 1 to 6 wherein a region of the device has at least one hydrophobic portion so that the flow of the deformable material is guided along a predetermined path.
8. An assay device (10) according to any of claims 1 to 7 wherein the deformable material is thermally deformable.
9. An assay device (10) according to any of claims 1 to 7 wherein the deformable material is mechanically deformable.

ART 34 AMDT

17

10. An assay device (10) according to any of claims 1 to 9 further including heating means (80).
11. An assay device (10) according to any of claims 1 to 10 further including a means for removing heat.
12. An assay device (10) according to any of claims 1 to 11 wherein the at least one surface defined by or in the device is resiliently deformable.
13. An assay device (10) according to any of claims 1 to 12 wherein a plurality of volumes of deformable material are provided, each volume being accessible independently one from another.
14. An assay device (10) according to any of claims 1 to 13 having at least one component from the set of: an inlet port (12), a reaction chamber (14), a waste depot (16), a filter chamber (18), an infinity capture and processing chamber (20), a wash solution/reagent reservoir (22), an array of metered readout cells (26,28,30,32), and a breather tube (11, 13).
15. An assay device (10) according to any of claims 1 to 14, in which heat is selectively applied to one or more of the volumes of the deformable material.
16. An assay device (10) according to any of claims 1 to 15, in which heat is selectively removed from one or more volumes of the deformable material.
17. An assay device (10) according to any of claims 1 to 16, in which pressure is selectively applied to at least one region contained within the device.
18. An assay device (10) having: a) at least one chamber (14) in fluid connection with at least one pathway (14a, 14b), the at least one pathway being adapted to allow fluid to flow to/from said at least one chamber (14); b) a volume of deformable material (46) situated in the pathway (14b) which, in use, changes its state so as to cause a change of the rate of fluid flow along the pathway; and c) at least one hydrophobic portion which defines a path along which the deformable material is guided.

ART 34 AMDT

19. An assay device (10) having: a) at least one chamber (14) in fluid connection with at least one pathway (14a, 14b), the at least one pathway being adapted to allow fluid to flow to/from said at least one chamber (14); b) at least one recess located substantially adjacent the pathway; c) a volume of deformable material (44) situated in the recess which, in use, changes its state so as to cause a change of the rate of fluid flow along the pathway; and d) at least one hydrophobic portion which defines a path along which the deformable material is guided.
20. A method of manufacturing the assay device (10) of any of claims 1 to 19, including the steps of: a) defining at least one fluid pathway (14a) on a substrate; b) defining at least one reaction chamber (14) on a substrate; c) forming at least one component composed of a deformable material (44) in the device; and d) bonding together at least two substrates to form the device (10).
21. A method of manufacturing the device (10) according to claim 20, wherein the at least one fluid pathway (14a) may be formed by: a) printing, b) etching, c) ablation, d) use of a mould, e) cutting, or a combination of any of steps a) to e).
22. A method of manufacturing the device (10) according to claim 20, wherein the at least one reaction chamber (14) is formed by: a) printing, b) etching, c) ablation, d) use of a mould, e) cutting, or a combination of any of steps a) to e).
23. A method of manufacturing the device (10) according to claim 20, wherein the at least one component (44) composed of a deformable material is formed by: a) printing of the deformable material onto the substrate, b) etching, c) pick-and-placing of components, d) injection of molten material into device using feeder tubes, or a combination of steps a) to d).
24. A method of manufacturing the device (10) according to claim 20, wherein the at least one substrate is bonded by: a) adhesives, b) curing, c) mechanical fixing, d) heating, e) anodic bonding, or a combination of steps a) to e).
25. Apparatus for varying the rate of fluid flow along a pathway (75), the apparatus including at least one pathway (75) and a volume of deformable material (78) disposed within the pathway whereby, in use, a change of state of the deformable material causes a change of the rate of fluid flow along the pathway.

ART 34 AMDT

19

26. Apparatus for varying the rate of fluid flow along a pathway (75), the apparatus including at least one pathway (75) and a volume of deformable material (78) disposed adjacent the pathway whereby, in use, a change of state of the deformable material causes a change of the rate of fluid flow along the pathway.
27. Apparatus according to claim 25 or 26 further including at least one chamber in fluid connection with the pathway.
28. Apparatus according to claim 27 wherein a volume of deformable material is disposed within the chamber.
29. Apparatus according to any of claims 25 to 28 wherein at least one recess (72) capable of receiving deformable material is located substantially adjacent the pathway (75).
30. Apparatus according to claim 29 wherein the at least one recess (72) has an opening (74) which acts as a vent in order to permit the flow of gas therethrough.
31. Apparatus according to any of claims 25 to 30 including at least one hydrophobic region (76) in order to guide fluid along a predetermined path.
32. Apparatus according to any of claims 25 to 31 including means for the supply and/or removal of heat from the apparatus in order to increase or decrease the rate of change of state of the deformable material.
33. Apparatus according to any of claims 25 to 32 including means for the supply of (i) pressure, (ii) uv radiation, (iii) light, (iv) ultrasonic energy or a combination of any of (i) to (iv) to the apparatus in order to change the state of the deformable material.
34. Apparatus according to any of claims 25 to 33 wherein the deformable material (78) includes a polymer.
35. Apparatus according to any of claims 25 to 33 wherein the deformable material (78) includes polypropylene polystyrene.
36. Apparatus according to any of claims 25 to 30 including at least one hydrophobic portion (76) which defines a path along which deformable material is guided.

ART 34 AMDT

37. Apparatus for varying the rate of fluid flow along a pathway (75), the apparatus including:

- a) at least one pathway (75); b) a volume of deformable material (78) disposed within the pathway, which, in use, changes its state so as to cause a change of the rate of fluid flow along the pathway; and c) at least one hydrophobic region (76) which defines a path along which deformable material is guided.

38. Apparatus for varying the rate of fluid flow along a pathway (75), the apparatus including:

- a) at least one pathway (75); b) a volume of deformable material (78) disposed adjacent the pathway, which, in use, change its state so as to cause a change of the rate of fluid flow along a pathway; and c) at least one hydrophobic region (76) which defines a path along which deformable material is guided.

39. A method of varying the rate of fluid flow along a pathway (75) comprising the steps of:

providing at least one recess (72) located substantially adjacent the pathway (75); locating a plug of deformable material (78) in the pathway so that the material substantially restricts the flow of fluid in the pathway; and changing the state of the deformable material so that at least a portion of the material passes into the at least one recess thereby permitting flow of the fluid along the pathway.

40. A method of varying the rate of fluid flow along a pathway comprising the steps of:

providing at least one recess (72) located substantially adjacent the pathway (75); locating a volume of deformable material (78) in the at least one recess; and changing the state of the deformable material so that at least a portion of the material passes into the pathway thereby substantially restricting flow of the fluid along the pathway.

41. A method of varying the rate of fluid flow along a pathway (75) comprising the steps of:

providing a pathway (75); locating a volume of deformable material (78) in the pathway so that it substantially restricts the flow of fluid along the pathway (75); and changing the state of the deformable material so that at least a portion of the material (78) passes along a predetermined path thereby permitting flow of the fluid along the pathway.

42. A method of varying the rate of fluid flow along a pathway (75) comprising the steps of:

providing a pathway (75); locating a volume of deformable material (78) in the pathway so that it substantially permits the flow of fluid along the pathway; and changing the state of the deformable material so that at least a portion of the material (78) passes along a predetermined path thereby substantially restricting flow of the fluid along the pathway.

43. A method according to claim 41 or claim 42 wherein the predetermined path is defined by one or more hydrophobic regions (76).
44. A method according to claims 39 to 42 whereby the state of the deformable material (78) is changed by applying to said material (i) heat, (ii) pressure, (iii) uv radiation, (iv) light, (v) ultrasonic energy or a combination of any of (i) to (v).
45. A method of varying the rate of fluid flow along a pathway (75) comprising the steps of: providing at least one recess (72) located substantially adjacent the pathway (75); locating a plug of deformable material (78) in the pathway so that the material substantially restricts fluid flow in the pathway; and changing the state of the deformable material so that at least a portion of the material passes along a predetermined path into the at least one recess thereby permitting flow of the fluid along the pathway, wherein the predetermined path is defined by one or more hydrophobic regions.
46. A method of varying the rate of fluid flow along a pathway comprising the steps of: providing at least one recess (72) located substantially adjacent the pathway (75); locating a volume of deformable material (78) in the at least one recess; and changing the state of the deformable material so that at least a portion of the material passes along a predetermined path into the pathway thereby substantially restricting flow of the fluid along the pathway, wherein the predetermined path is defined by one or more hydrophobic regions.
47. A method of varying the rate of fluid flow along a pathway (75) comprising the steps of: providing a pathway (75); locating a volume of deformable material (78) in the pathway so that it substantially restricts fluid flow along the pathway (75); and changing the state of the deformable material so that at least a portion of the material (78) passes along a predetermined path thereby permitting flow of the fluid along the pathway, wherein the predetermined path is defined by one or more hydrophobic regions.
48. A method of varying the rate of fluid flow along a first pathway (75) comprising the steps of: providing a first pathway (75); locating a volume of deformable material (78) in the first pathway; flowing a fluid along the first pathway past the material; and changing the state of the material so that at least a portion of the material (78) passes along a second pathway so as to restrict fluid flow along the first pathway, said second pathway being defined by one or more hydrophobic regions.

21a

49. An assay device (10) substantially as described with reference to Figure 1.
50. Apparatus substantially as described herein with reference to Figures 2 to 9.
51. A method of varying the rate of fluid flow along a pathway substantially as described herein with reference to the Figures.
52. A method of performing chemical analysis substantially as described with reference to the Figures.

09/623181

422 Rec'd PCT/PTO 29 AUG 2000

22

APPARATUS FOR, AND METHOD OF, VARYING THE
RATE OF FLOW OF FLUID ALONG A PATHWAY

ABSTRACT

5

An apparatus for varying the rate of flow of a fluid in a pathway by the use of deformable valves and clamps which change their size, position, state or function on application of heat and/or pressure is described. A disposable chemical assay device 10 (10), and a method of using the device incorporating the apparatus are also described. The assay device (10) includes an inlet port (12), a reaction chamber (14), a waste depot (16), a filter chamber (18), a processing chamber (20), wash solution/reagent reservoirs (22) and (24), an array of metered readout cells (26, 28, 30 and 32), and breather tubes (11 and 13). The invention, in a preferred embodiment, offers an 15 advantage over existing assay devices because the condition or state of the deformable valves and clamps may be changed. Therefore more complex operations and procedures may be performed by the assay device (10) than has been previously achievable.

20

(Figure 1)

1/6

Fig.1.

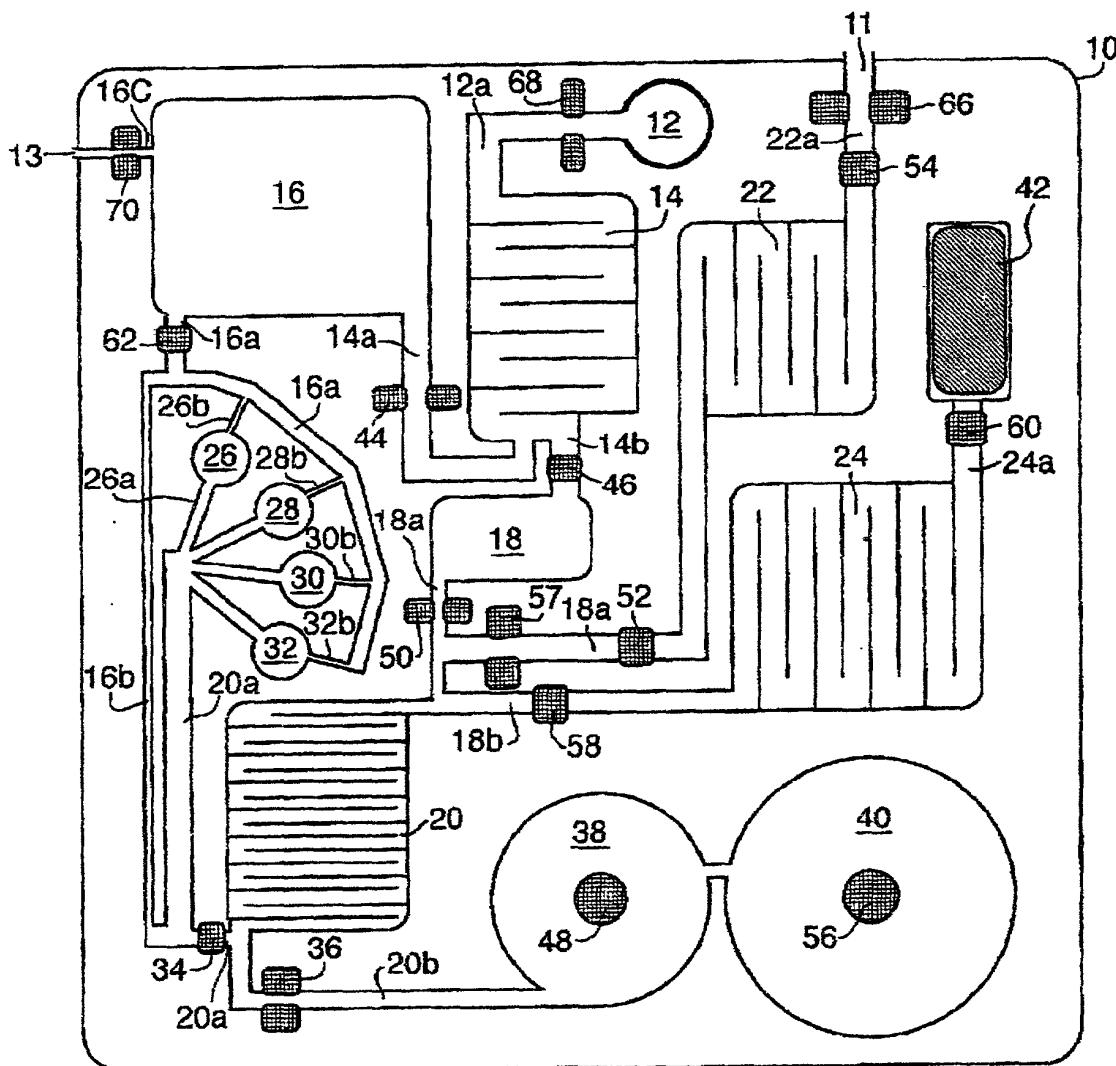


Fig.2a.

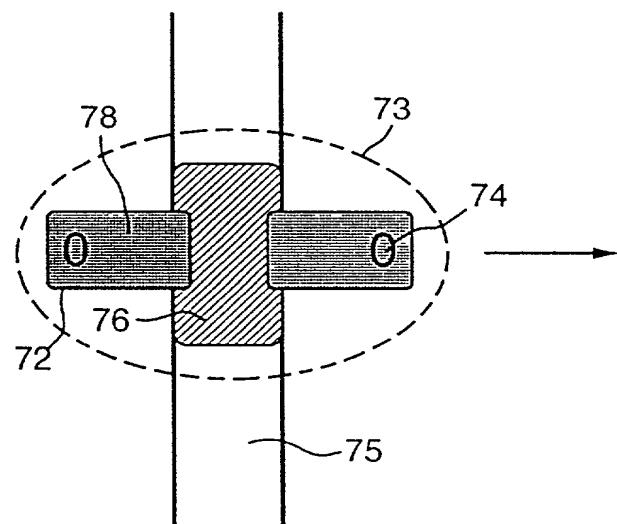


Fig.2b.

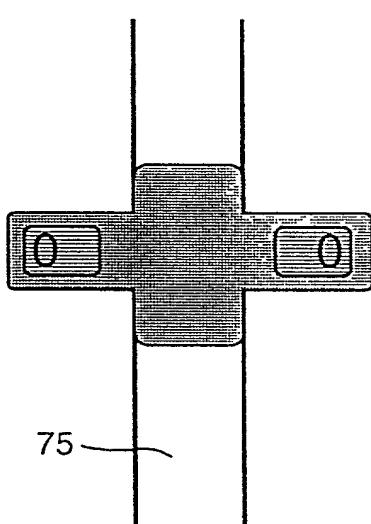


Fig.3a.

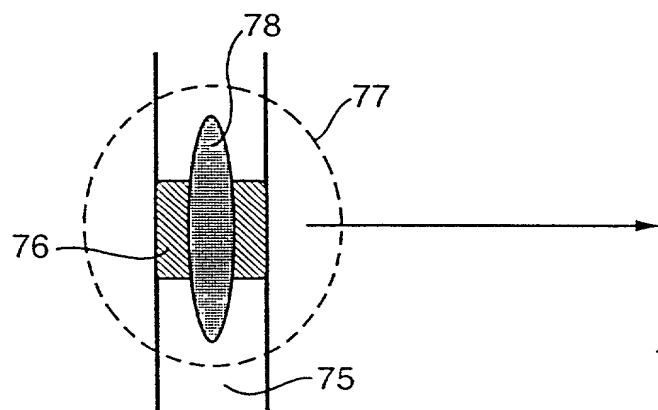
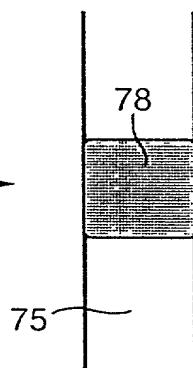


Fig.3b.



3/6

Fig.4a.

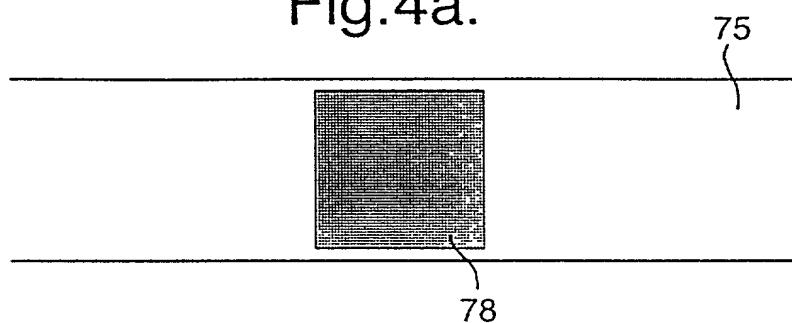


Fig.4b.

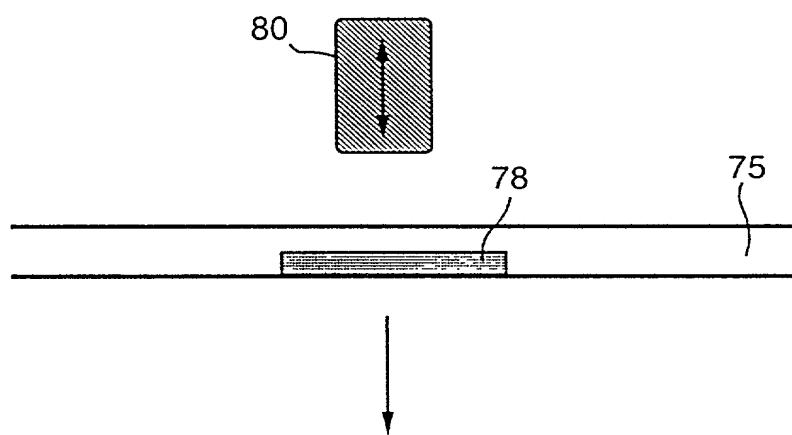


Fig.4c.

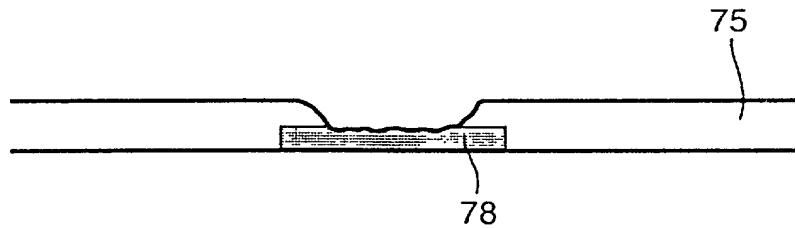


Fig.5a.

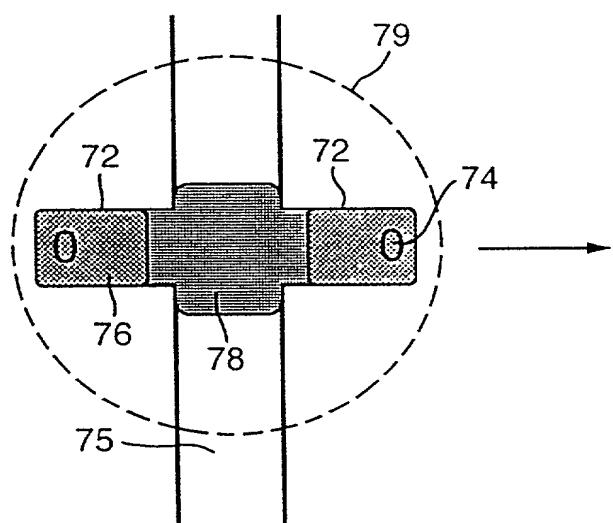


Fig.5b.

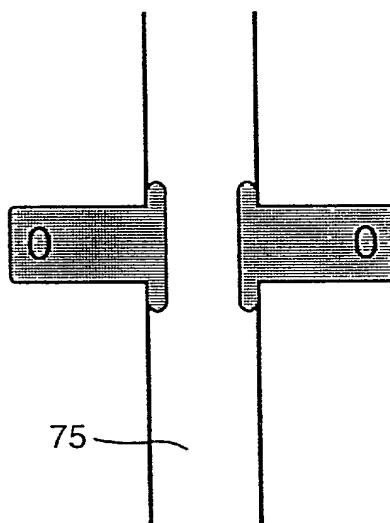


Fig.6a.

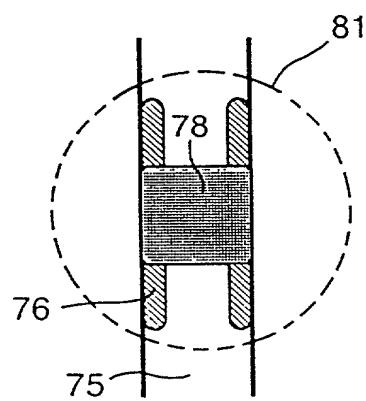
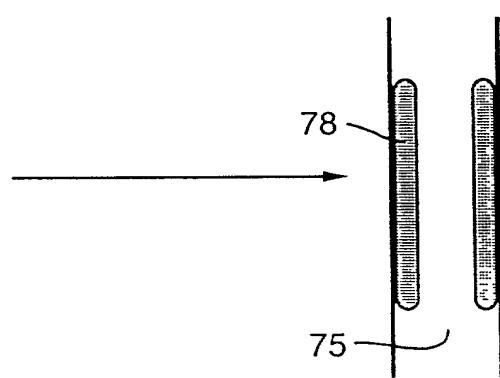
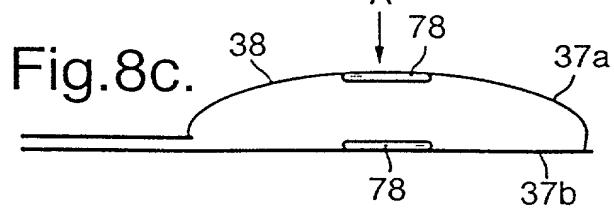
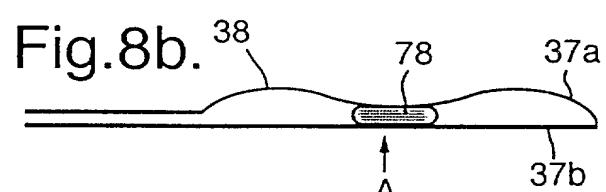
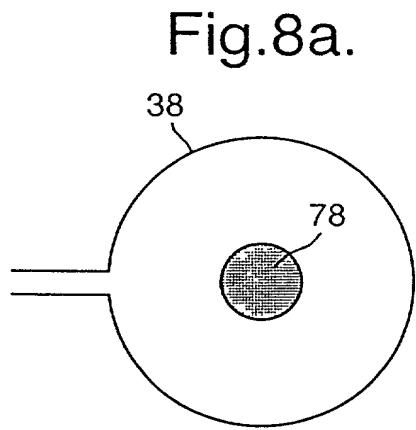
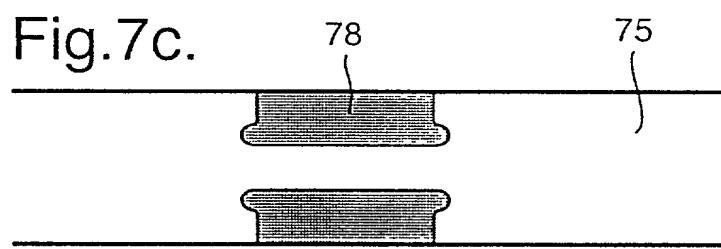
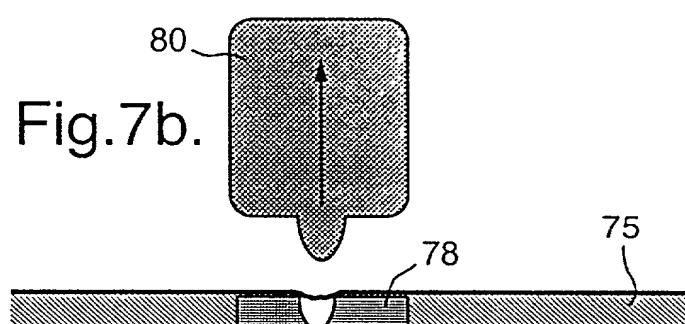
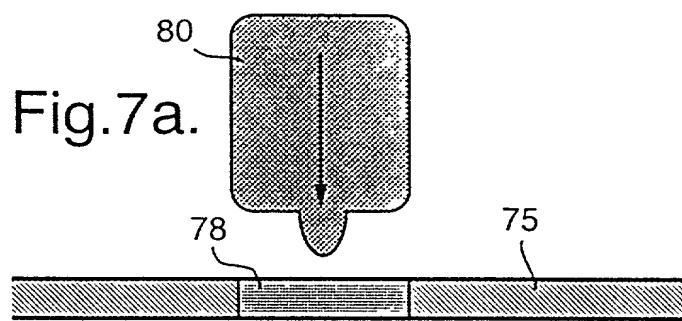


Fig.6b.



5/6



6/6

Fig.9a.

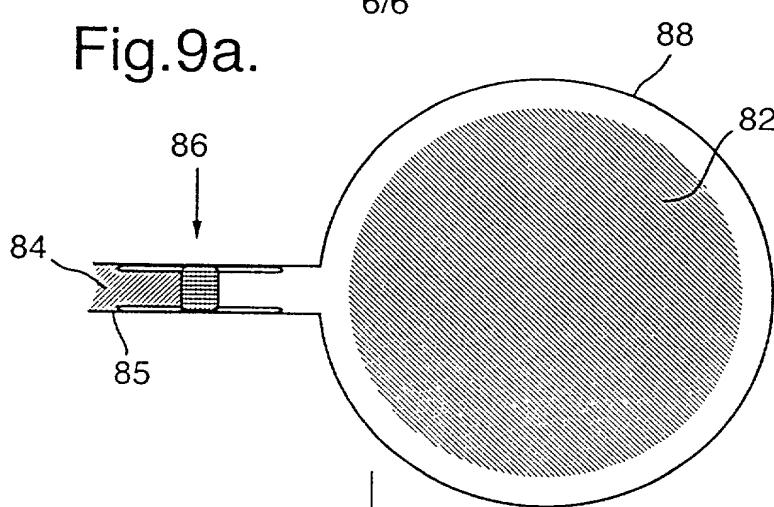


Fig.9b.

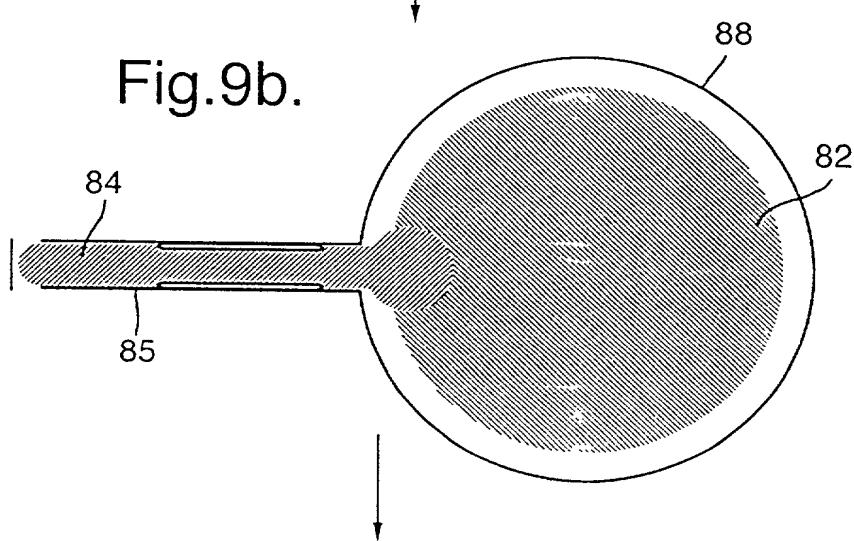


Fig.9c.

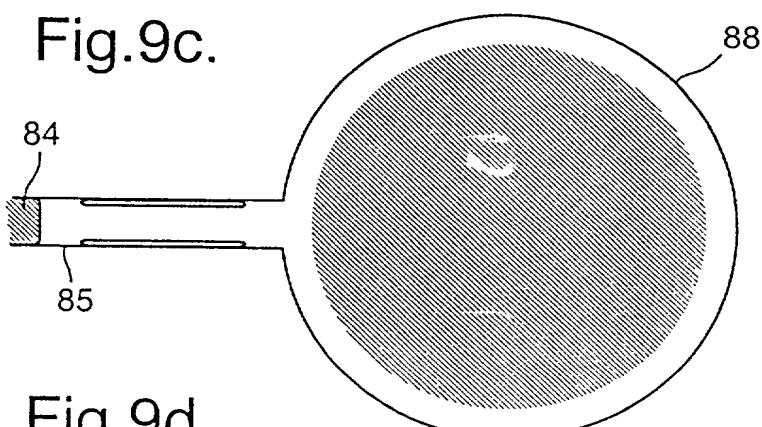
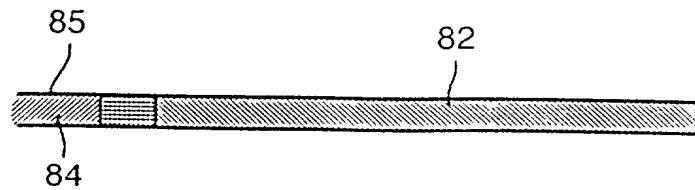


Fig.9d.



IN THE UNITED STATES
PATENT AND TRADEMARK OFFICE

Declaration and Power of Attorney (Sole Inventor)

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name.

I believe that I am the original, first and sole inventor of the subject matter which is claimed and for which a patent is sought on the invention entitled Apparatus for, and method of, varying the rate of flow of fluid along a pathway

the specification of which; is being filed herewith.

was filed on _____.

I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by an amendment, if any, specifically referred to in this oath or declaration.

I acknowledge the duty to disclose all information known to me which is material to patentability as defined in Title 37, Code of Federal Regulations, 1.56.

I hereby claim foreign priority benefits under Title 35, United States Code, 119 of any foreign application(s) for patent or inventor's certificate listed below and have also identified below any foreign application for patent or inventor's certificate having a filing date before that of the application on which priority is claimed:

I hereby claim the benefit under Title 35, United States Code, 120 of any United States application(s) listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States application in the manner provided by the first paragraph of Title 35, United States Code, 112, I acknowledge the duty to disclose all information known to me to be material to patentability as defined in Title 37, Code of Federal Regulations, 1.56 which became available between the filing date of the prior application and the national or PCT international filing date of this application:

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

I hereby appoint the following attorneys with full power of substitution and revocation, to prosecute said application, to make alterations and amendments therein, to receive the patent, and to transact all business in the Patent and Trademark Office connected therewith:

5 -

William H. Bollman	(Reg. No. 36,457)
W. Warren Taltavull	(Reg. No. 25,647)
Edward J. Stemberger	(Reg. No. 36,017)
Jeffrey S. Melcher	(Reg. No. 35,950)
Ki S. Kim	(Reg. No. 43,450)

Please address all correspondence to:

William H. Bollman
FARKAS & MANELLI PLLC
2000 M Street, N.W. Suite 700
Washington, DC 20036-3307
TEL: (202)261-1000
FAX: (202)887-0336

Please direct all telephone calls to:

William H. Bollman at (202) 261-1020.

1-00 Full name of sole inventor: John Edward Andrew Shaw

Inventor's signature

Date: 27/11/00

Residence: West Drayton, Middlesex, UB7 7BL, England EN8.

Citizenship: British ✓

Post Office Address: 45 Colne Avenue, West Drayton, Middlesex, UB7 7AL, England